Remarks

This communication responds to the Office Action mailed October 24, 2006, for the application captioned above, the period for response to which has been extended to April 24, 2007 by the accompanying Petition for Extension of Time. Claims 1-28 were pending. Claims 1-4 and 7-13 are withdrawn from consideration, and have now been cancelled without prejudice, together with claims 27 and 28, to facilitate the prosecution of this case. Claims 5, 6, and 14-28 are rejected. Claims 6, 14, and 22-25 have been amended and new claims 29-31 have been added above. Claims previously shown as withdrawn have now been cancelled without prejudice, in order to facilitate the prosecution of this case. Upon entry of this Amendment, Claims 6, 14-26 and 29-31will be pending and in condition for allowance.

Claims 5, 6, and 14-28 stand rejected under 35 U.S.C. 112, second paragraph. The claims have been editorially amended to address the Examiner's concerns. In particular, claim 5 has been rewritten as new claim 29, in a manner that avoids the use of terms such as "capable" and "means", and that clarifies various other matters. Similarly, claims 27 and 28 have been provided as new dependent claims 30 and 31, to address similar concerns. It should be noted that the term "xenogenic serum" remains, and will be quite clear to those skilled in the art, as indicating that the final suspension is substantially free of foreign matter.

The present invention relates to a unique cell suspension for use in grafting, including a method of preparing and a method of using such a suspension. The suspension is prepared by a method that includes obtaining tissue sample, dissociating cells from the sample, harvesting the dissociated cells, and filtering and optionally diluting the harvested cells to form a suspension that can be used to treat a patient in need of a graft. In turn, the resulting suspension can provide an array of benefits as compared to previous approaches, including an optimal combination of time and ease of preparing the suspension, and in turn, the time and flexibility of its use.

The Office Action focuses largely on the fact that the pending claims provide a product by process, and also, that they include various terms including the word "means". For these and other reasons, the Action states (e.g., at page 7) that claim 5 are being interpreted as including little more than a solution of dissociated cells in a nutrient solution, lacking large aggregates. In

other words, the Action is giving essentially no patentable weight to what are clearly the key features of this invention. In turn, there is little doubt that the Action would readily find an array of references that it considers to teach the few and minimal aspects it currently interprets as being the claims.

New claims 29-31 address the Examiner's concerns, and now clearly provide unique features of the suspension, brought about as a result of the method of its preparation, though now in a manner that must be accorded patentable weight. These include the fact that the suspension is a) free of xenogenic serum and b) cell conglomerates, c) the cells remain viable, and d) the suspension is suitable for direct application to a region on a patient undergoing tissue grafting.

The array of references cited fail in at least one, and generally several ways, to teach or suggest these and other various features of the invention. For instance, none of the cited references appear to teach the direct application of a cell suspension, or in turn, the preparation and use of a cell suspension for grafting. In addition, neither Osborne, Noel-Hudson, Suzuki teach the presence of a xenogenic serum, and Katz is quite uncertain in this respect. Moreover, neither Gunawardana, Lucas, Suzuki, or Katz appear to describe the use of keratinocytes at all.

In particular, Claims 5, 6, and 14-24 stand rejected under 35 U.S.C. 102(b) as being anticipated by Yannas et al. (U.S. Patent No. 4,418,691). This document teaches a technique following the method of Green. However, the cells are then placed into a template for subsequence application to a defect. The cells are expanded in culture prior to the secondary harvest. The method of the present invention does not require these steps.

Claims 5, 6, 14-21, and 23-28 stand rejected under 35 U.S.C. 102(b) as being anticipated by Suzuki et al. (EP 0 350 887). The serum free method for cardiac muscle cells described in this application is not applicable to keratinocytes.

Claims 5, 6, and 14-28 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hirobe (Journal of Cellular Physiology, 152: 337-345, 1992). Hirobe describes the role of epidermal components in the induction of melanocyte differentiation by Melanocyte Stimulating Hormone (MSH). In particular, the focus of this article was to investigate which substances produced by keratinocytes were responsible for regulating the proliferation of mammalian melanocytes. Although Hirobe suggest that the culture system was serum free, on page 338,

column 1, paragraphs 1 and 2, the primary culture mediums developed for culturing keratinocytes and melanocytes both contain Bovine Serum Albumin (BSA) at a concentration of 1 mg/ml. In addition, the method of cell culture requires culturing of the cells for up to 12 days, replacing the medium four times per week.

In contrast, the present application discloses a nutrient solution free from xenogenic (e.g. BSA) serum. The present invention discloses a unique cell suspension and method for its preparation that is rapid, efficient and simple to prepare and apply. The inventors have also found that by removing xenogenic serum from the cell suspension, there is less chance of transmission of infection and reaction between a patient and the serum. Further, the tissue sample used to isolate the cells in the suspension is removed from the enzyme solution (e.g. trypsin) before the cells are harvested.

Claims 5, 6, and 14-28 stand rejected under 35 U.S.C. 102(b) as being anticipated by Noel-Hudson et al., In Vitro Cell and Developmental Biology - Animal 31: 508-515, 1993. Noel-Hudson, et al (1995) relates to the technique of harvesting cells for the development of skin constructs, by seeding human keratinocytes onto culture cell membranes. The method of Noel-Hudson, et al, is not designed for the use of cells in a suspension for treatment of a wound.

More specifically, the methods and materials section of the cited document teaches cells and culture conditions, which involved the following steps: (i) obtaining a tissue sample, (ii) treating the tissue sample with trypsin in a nutrient media for 2 hours at 37°C, (iii) further trypsin treatment to release individual cells, (iv) cultivation of isolated keratinocytes in collagen 1 coated Petri dishes and (v) a washing step. The cells were then applied to the membranes for the experimental study of cell growth.

In contrast, the apparatus of the present invention provides a unique device for preparing cell suspensions in a limited environment. That is, it provides a time efficient method for supplying a cellular cover to a tissue in a clinical setting. For example, cells are available when needed at the time of surgery. This is achievable because there is a very short preparation period of the cells, thus allowing grafting to be performed peri-operatively or in the rooms of a specialist physician or General Practitioner.

In addition, the present invention provides an apparatus which significantly reduces the complexity associated with the use of conventional Cultured epithelial autografts and is particularly useful in cases of burn injury that have presented late. In some instances, cells are unavailable at the time of surgery, either due to delayed referral of a patient with an unhealed burn or simply because the time needed for culturing of the grafts had exceeded that for preparation of the recipient would bed. The present invention ameliorates the issue of graft preparation time.

Claims 5, 6, 14-21, 23, and 24 stand rejected under 35 U.S.C. 102(b) as being anticipated by Gunawardana et al. (U.S. Patent No. 5,352,806). This has no relevance to the preparation or use of cell suspension therapy as it is directed towards compounds having a chemical formula.

Claims 5, 6, and 14-28 stand rejected under 35 U.S.C. 102(b) as being anticipated by Lucas et al. (U.S. Patent No. 5,328,695). This document discloses a system of stimulating cells not using cells as a direct therapy.

Claims 5, 6, and 14-28 stand rejected under 35 U.S.C. 102(b) as being anticipated by Lavker et al. (U.S. Patent No. 5,556,783). This document teaches a suspension of cells that are harvested from cell culture on 3T3 according to the known method of Green. That is the cells require a layer of feeder cells. This is one of the steps which the method of the present application does not require.

Claims 5, 6, and 14-21 stand rejected under 35 U.S.C. 102(b) as being anticipated by Katz et al. (U.S. Patent No. 5,786,207). The document discloses a tissue dissociating system and methods for use. The document neither teaches nor suggests a cell suspension therapy as taught in the pending claims.

Claims 5, 6, and 14-28 stand rejected under 35 U.S.C. 102(b) as being anticipated by Osborne et al., Biomaterials 20: 283-290 (1999). This paper describes a 3D composite skin reconstruction. The cells are passaged three times, and the process requires the use of a dispase/trypsin combination, prior to use.

Claims 5, 6, and 14-28 stand rejected under 35 U.S.C. 102(e) as being anticipated by Dennis et al. (U.S. Patent No. 6,207,451). This document does not use cell suspension as a direct therapy. It is focused on the 3D muscle organisation *in vitro*.

Reconsideration of the rejections and allowance of all pending claims at an early date is respectfully requested.

Respectfully submitted,

Dated: April 24, 2007

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